

What we claim is:

1. A modified protein or polypeptide or a salt thereof comprising a protein or polypeptide conjugated by an intermediate group containing at least one radical having the formula $-C(R)=N-$, $-N=C(R)-$, $-CH(R)-NH-$ or $-NH-CH(R)-$, in which R is hydrogen or an aliphatic, cycloaliphatic, aromatic or araliphatic hydrocarbon group, which group may be substituted with the same or a different protein or polypeptide, a reporter group or a cytotoxic agent.

10

2. The modified protein or polypeptide of claim 1 in which the radical is $-CH=N-$, $-N=CH-$, $-CH_2-NH-$ or $-NH-CH_2-$.

15 3. The modified protein or polypeptide of claim 1 having the formula



20 in which

A is a residue of a protein or polypeptide;

B is a residue of a protein or polypeptide, a reporter group or a cytotoxic agent;

25 X and X' independently from each other are bivalent organic radicals or may be absent;

Z is a bivalent radical selected from the group consisting of $-C(R)=N-$, $-N=C(R)-$, $-CH(R)-NH-$, $-NH-CH(R)-$, $-C(R)=N-Y-N=C(R)-$, $-N=C(R)-Y-C(R)=N-$,

30 $-CH(R)-NH-Y-NH-CH(R)-$ and $-NH-CH(R)-Y-CH(R)-NH-$, where R is hydrogen or an aliphatic, cycloaliphatic, aromatic or araliphatic hydrocarbon group, which group may be substituted with the same or a different protein or polypeptide, a reporter group or a cytotoxic agent, with at least one aromatic radical or oxygen adjacent to nitrogen; and

35

Y is a bivalent organic group.

4. The modified protein or polypeptide of claim 3 in which Z is a bivalent radical selected from the group consisting of $-C(R)=N-O-$, $-O-N=C(R)-$, $-CH(R)-NH-O-$, $-O-NH-CH(R)-$, $-C(R)=N-O-Y-O-N=C(R)-$, $-O-N=C(R)-Y-C(R)=N-O-$, $-CH(R)-NH-O-Y-O-NH-CH(R)-$ and $-O-NH-CH(R)-Y-CH(R)-NH-O-$.

5

5. The modified protein or polypeptide of claim 1 having the formula



10

in which

A is a residue of a protein or polypeptide;

B is a residue of a protein or polypeptide, a

15 reporter group or a cytotoxic agent;

X and X' independently from each other are bivalent organic radicals or may be absent;

Z is a bivalent radical selected from the group consisting of $-CH=N-$, $-N=CH-$, $-CH_2-NH-$, $-NH-CH_2-$,

20 $-CH=N-Y-N=CH-$, $-N=CH-Y-CH=N-$, $-CH_2-NH-Y-NH-CH_2-$ and $-NH-CH_2-Y-CH_2-NH-$, with at least one aromatic radical or oxygen adjacent to nitrogen; and

Y is a bivalent organic group.

25 6. The modified protein or polypeptide of claim 3 in which A is connected to $X-Z-X'-B$ by its carboxy terminus.

7. The modified protein or polypeptide of claim 3 in which A is connected to $X-Z-X'-B$ by a side chain.

30

8. The modified protein or polypeptide of claim 3 in which A is connected to $X-Z-X'-B$ by its amino terminus.

35

9. The modified prot in or polypeptide of claim 3 in which Z is $-C(R)=N-$ or $-N=C(R)-$.

10. Th modified protein or polypeptide of claim 4 in which Z is $-C(R)=N-O-$ or $-O-N=C(R)-$.

5

11. The modified protein or polypeptide of claim 5 in which Z is $-CH_2-NH-$ or $-NH-CH_2-$.

12. The modified protein or polypeptide of claim 5 in
10 which an aromatic radical is adjacent to the N-atom of the Z group which is $-N=CH-$ or $-NH-CH_2-$.

13. The modified protein or polypeptide of claim 5 in which Z is $-CH=N-Y-N=CH-$ or $-N=CH-Y-CH=N-$.

15

14. The modified protein or polypeptide of claim 5 in which Z is $-CH_2-NH-Y-NH-CH_2-$ or $-NH-CH_2-Y-CH_2-NH-$.

15. The modified protein or polypeptide of claim 13 in
20 which Y is a phenylene radical.

16. The modified protein or polypeptide of claim 14 in which Y is a phenylene radical.

25 17. The modified protein or polypeptide of claim 5 in which an aromatic group is directly adjacent to the N-atoms of the Z group which is $-N=CH-Y-CH=N-$ or $-NH-CH_2-Y-CH_2-NH-$.

30 18. The modified protein or polypeptide of claim 5 in which X or X' is a phenylene radical.

19. The modified protein or polypeptide of claim 5 in which both X and X' are phenylene radicals.

35

20. The modified protein of claim 1 in which the protein is an immunoglobulin or a fragment thereof.

21. The modified protein of claim 20 in which the protein is an IgG molecule or a fragment thereof.

22. The modified protein of claim 20 in which the protein is an Fab or F(ab')₂ fragment of an immunoglobulin.

23. The modified protein or polypeptide of claim 1 in which the reporter group is a residue of desferrioxamine B or a metal derivative thereof.

24. The modified protein or polypeptide of claim 1 in which the reporter group is a residue of DTPA or a metal derivative thereof.

25. The modified protein or polypeptide of claim 1 in which the reporter group is -[N^C-(DTPA-alanyl)-Lys]₅ or a metal derivative thereof.

26. The modified protein or polypeptide of claim 1 in which the reporter group is polyglutamic acid residue to which several ferrioxamine^B residues have been coupled.

27. The modified protein or polypeptide of claim 1 which is a drug or a diagnostic tool.

28. A modified protein or polypeptide having the formula



in which A is a residue of a protein or polypeptide;

X is a bivalent organic radical or may be absent; and
R^{1'} is a -CO-R, acetalized formyl, amino or protected amino group, where R is hydrogen or an aliphatic, cycloaliphatic, aromatic or aliphatic hydrocarbon group, which group may be substituted with the same or a different protein or polypeptide, a reporter group or a cytotoxic agent.

10

29. The modified protein or polypeptide of claim 28 in which R^{1'} is a formyl, acetalized formyl, amino or protected amino group.

15

30. The modified protein or polypeptide of claim 28 in which X contains an aromatic group directly adjacent to R^{1'}.

20

31. The modified protein or polypeptide of claim 28 in which X is -NH-C₆H₄-.

32. The modified protein or polypeptide of claim 28 in which X is -NH-CH(COOCH₃)-CH₂-C₆H₄-.

25

33. The modified protein or polypeptide of claim 28 in which X is -NH-CH(CONH₂)-CH₂-C₆H₄-.

34. The modified protein or polypeptide of claim 28 in which A is an immunoglobulin or a fragment thereof.

30

35. The modified protein or polypeptide of claim 34 in which A is an IgG molecule or a fragment thereof.

35

36. The modified protein or polypeptide of claim 34 in which A is an Fab or F(ab')₂ fragment of an immunoglobulin.

37. A compound having the formula



- 5 in which B' is a residue of DTPA, ferri xamine B or desferrioxamine B, cuprioxamine B, polyglutamic acid and derivatives thereof or $[N^{\epsilon}(\text{DTPA-alanyl})\text{-Lys}]_n$, with n being an integer >1;
- 10 X' is a bivalent organic group or may be absent; and
- 15 R^{2'} is a -CO-R, -O-NH₂, acetalized formyl, amino or protected amino group, where R is hydrogen or an aliphatic, cycloaliphatic, aromatic or araliphatic hydrocarbon group, which group may be substituted with the same or a different protein or polypeptide, a reporter group or a cytotoxic agent.

20 38. The compound of claim 37 in which B' is a residue of DTPA, ferrioxamine B or desferrioxamine B, cuprioxamine B or $[N^{\epsilon}(\text{DTPA-alanyl})\text{-Lys}]_n$, with n being an integer >1.

25 39. The compound of claim 37 in which R^{2'} is a formyl, acetalized formyl, amino or protected amino group.

40. The compound of claim 37 in which R^{2'} is -O-NH₂.

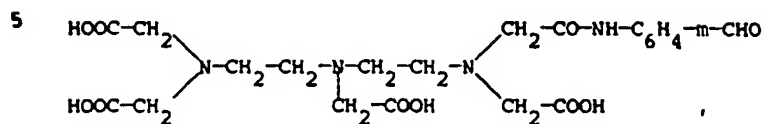
30 41. The compound of claim 37 which is N-(m-amino-benzoyl)-ferrioxamine B.

42. The compound of claim 37 which is N-(m-amino-benzoyl)-cuprioxamine B.

35 43. The compound of claim 37 which has the formula $m\text{-H}_2\text{N-C}_6\text{H}_4\text{-CO-[N}^{\epsilon}(\text{DTPA-alanyl})\text{-Lys}]_n$, in which n is an integer >1.

44. The compound of claim 43 in which n is 5.

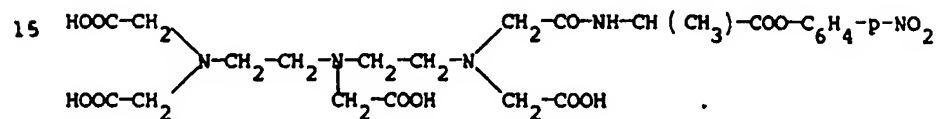
45. The compound of claim 43 which is DTPA-mono-(m-formylanilide), having the formula



or an acetal thereof.

10

46. The compound of claim 43 which is DTPA-alanine-p--nitrophenylester, having the formula



20

25

30

35

43530